UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,238	01/19/2006	Pnina Fishman	FISHMAN19B	9164

1444 7590 05/08/2009

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
SINGH, SATYENDRA K	
ART UNIT	PAPER NUMBER
1657	
MAIL DATE	DELIVERY MODE
05/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,238	FISHMAN ET AL.	
	Examiner	Art Unit	
	SATYENDRA K. SINGH	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-28* is/are pending in the application.

4a) Of the above claim(s) *22-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response and amendments to claims filed on 02/09/2009 is duly acknowledged.

Claims 15-20 (elected invention of group III) and newly added claims 21-28 are currently pending in this application.

Election/Restrictions

Newly submitted claims 22-28 are directed to an invention that is independent or distinct from the invention originally claimed (group III) and elected for examination for the following reasons:

Group III. Claims 15-20 and newly added claim 21(as currently amended), directed to a method for selecting a subject in an inflammatory state, which subject is suitable for anti-inflammatory therapeutic treatment by means of an A3 adenosine receptor agonist, as specifically recited in claim 15.

Group IV: newly added Claims 22-28, directed to a method for determining the probability that a selected subject in an inflammatory state will respond to anti-inflammatory therapeutic treatment by means of an A3 adenosine receptor (A3AR) agonist, as specifically recited in claim 22.

> NOTE: Applicants are advised that newly added **claim 27**, though depends from claim 15 of group III, has been grouped together with the invention of group IV, because the claim is directed to the subject matter of claim 22 as currently recited "…for determining the probability that said subject is a candidate for receiving anti-inflammatory therapeutic treatment under clinical studies, wherein said determining step comprises determining that there is a greater probability that the subject is a candidate for receiving said anti-inflammatory therapeutic treatment under clinical studies if said level is above a predefined threshold that is above the level of A3AR expression in WBCs of a healthy subject."

The inventions of groups III and IV are directed to two separate and distinct processes. The invention of Group III (originally elected invention) is directed to a method for selecting a subject in an inflammatory state, which subject is suitable for anti-inflammatory therapeutic treatment by means of an A3 adenosine receptor agonist, as specifically recited in claim 15, whereas the invention of group IV is directed to a method for determining the probability that a

selected subject in an inflammatory state will respond to anti-inflammatory therapeutic treatment by means of an A3 adenosine receptor (A3AR) agonist, as specifically recited in claim 22. These methods are distinct both physically and functionally, recite different purposes, require distinct method steps and produce different endpoints.

Since, the special technical feature (i.e. A3 adenosine receptor and its agonist) as claimed is known in the prior art (see previous office action dated 05/16/08, page 3, in particular), no special technical feature unites the multiple inventions (i.e. processes) as currently presented by the applicants.

Therefore, the restriction requirement is deemed to be proper and is made FINAL.

Applicant is advised that, since 37 CFR 1.142(a) provides that restriction is proper at any stage of prosecution up to final action, a second requirement may be made when it becomes proper, even though there was a prior requirement with which applicant complied. *Ex parte Benke, 1904 C.D.63, 108 O.G. 1588 (Comm'r Pat. 1904).*

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, newly added claims 22-28 are **withdrawn** from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 15-21 (elected invention of group III, as currently amended) have been examined on their merits in this office action.

The following contains **new ground of rejections** necessitated by applicant's current amendments to pending claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names **joint inventors**. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 15- 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gessi et al (September 2004; IDS; citation AS) taken with Rhodes & Campbell (2002; [U]) and in view of Montesinos et al (2003; IDS, citation AQ) and Fishman & Bar-Yehuda (2003; [V]).

Claims are directed to a method for selecting a subject in an inflammatory state, which subject is suitable for anti-inflammatory therapeutic treatment by means of an A3 adenosine receptor (A3AR) agonist the method comprising: determining the level of expression of A3AR in a sample of white blood cells (WBCs) of the subject and selecting the subject as being suitable to receive said anti-inflammatory therapeutic treatment if said level is above a predefined threshold that is above the level of A3AR expression in WBCs of a healthy subject; wherein said sample of WBC is taken from a subject before receiving an anti-inflammatory treatment; and

wherein said predefined threshold is a multiple of the level of A3AR expression in the WBCs of a healthy subject.

It is noted that applicants have disclosed the term "***inflammatory state***" as including the following (instant specification, page 6):

> "An "inflammatory state" includes any state of active or sub-clinical inflammation. By a preferred embodiment the invention is used for determining an inflammatory state in subjects suffering from and autoimmune inflammatory disease. The inflammation may be due to an inflammatory disease, or it may be a side effect of some other type of disease or disorder."

Gessi et al disclose a method for selecting a subject (i.e. a method for diagnosing a patient; see abstract, page 5895; "*Conclusions*", in particular) in an inflammatory state (see evidentiary prior art disclosure of Rhodes & Campbell, wherein they disclose colorectal cancer and its association with inflammation, and the fact that a patient suffering from colorectal cancer is a subject in "an inflammatory state"; see page 10, figure 2, pages 13 and 15, in particular), the method comprising: determining the level of expression of A3AR in a sample of white blood cells (WBCs) of the subject (see; Gessi et al, determination of A3AR levels by receptor binding assays in peripheral blood cells such as lymphocytes and neutrophils, protein levels confirmed by immunohistochemistry; page 5898, table 3, in particular), wherein said sample of WBC is taken from a subject before receiving an anti-inflammatory treatment (such as before a surgical resection; see Gessi et al, abstract, and page 5896, in particular); and wherein said predefined threshold is a multiple of the level of A3AR expression (3-fold in terms of receptor density when compared with healthy subjects; see Gessi et al, abstract, in particular) in the WBCs of a healthy subject (see also Gessi et al, page 5898, table 3 and figure 2, in particular).

However, the method step of selecting the subject as being suitable to receive said anti-inflammatory therapeutic treatment by means of an A3 adenosine receptor (A3AR) agonist if

said level is above a predefined threshold that is above the level of A3AR expression in WBCs of a healthy subject; and wherein the inflammatory state is result of an autoimmune disease such as **rheumatoid arthritis** (RA), is not explicitly disclosed by Gessi et al taken with Rhodes & Campbell.

Fishman & Bar-Yehuda disclose the pharmacology and therapeutic applications of A3 receptor subtype, especially the use of agonists such as IB-MECA (N6-(3-iodobenzyl)-adenosine-5'-N-methyluronamide; see page 463, abstract and introduction, in particular) as most potent therapeutic agents for the treatment of inflammation, wherein they disclose the fact that the anti-inflammatory response is mediated upon A3AR activation in neutrophils, eosinophils and macrophages (i.e. white blood cell components) via direct effect on the production of anti-inflammatory cytokines (see page 464, right column, in particular). Thus, Fishman & Bar-Yehuda clearly suggest the use of agonist such as IB-MECA for activation of A3AR receptor to produce desired anti-inflammatory effects in subjects in need thereof, including in clinical settings for therapeutic treatment.

Montesinos et al disclose the role of A3AR receptors, the activation of which is required for the inhibition of inflammation (i.e. for anti-inflammatory therapeutic treatment) by methotrexate commonly used for the therapy of chronic inflammatory diseases, including autoimmune joint disorders such as RA (see page 240, in particular).

Thus, given the detailed disclosures in the cited prior art at the time of claimed invention, it would have been obvious to a person of ordinary skill in the art to modify the method of Gessi et al such that the subject is selected as being suitable to receive said anti-inflammatory therapeutic treatment by means of an A3AR agonist if said level is above a predefined threshold that is above the level of A3AR expression in WBCs of a healthy subject, wherein the inflammatory state is result of an autoimmune disease such as rheumatoid arthritis, as clearly

suggested and implicated by the combined teachings of the cited prior art references of Fishman & Bar-Yehuda and Montesinos et al.

One of ordinary skill in the art would have been motivated to do such modification in the method of Gessi et al because the disclosures of both Fishman & Bar-Yehuda and Montesinos et al strongly implicate A3AR receptor activation and its role anti-inflammatory treatment in patients with inflammation (such as RA or other inflammatory diseases), especially using the well known A3AR agonists such as IB-MECA, with reasonable expectation of success (see disclosures of Fishman & Bar-Yehuda, in particular). Thus, an artisan of ordinary skill in the art, at the time this invention was made, would have fully contemplated the implications and teachings from the cited prior art that provide the nexus between the over-expression of A3AR receptor in peripheral white blood cells (such as lymphocytes, neutrophils, etc. as taught by Gessi et al) and inflammatory state of a subject that is suitable to receive the anti-inflammatory treatment (including as a candidate for treatment under clinical studies) by means of an A3AR agonist such as IB-MECA, as explicitly suggested in the cited prior art.

Thus, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the art at the time the claimed invention was made.

As per MPEP 2111.01, *during examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, F.3d, 2004 WL 1067528 (Fed. Cir. May 13, 2004)(The USPTO uses a different standard for construing claims than that used by district courts; during examination the USPTO must give claims their broadest reasonable interpretation.). This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz*, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

Response to Arguments

Applicant's arguments with respect to claims 15-21 (filed on 02/02/2009) have been considered but are **moot** in view of the new ground(s) of rejection made in this office action.

Conclusion

NO claims are allowed.

Pertinent prior art not relied upon in the Rejection:

1. Fishman (US 2003/0143282 A1; July 31, 2003) – Adenosine A3 receptor agonist.
2. Liang et al. (US 6,211,165 B1; issued on April 3, 2001) - Methods and compositions for reducing ischemic injury of the heart by administering adenosine receptor agonists and antagonists.
3. Jacobson et al. (US 5,646,156; issued on July 8, 1997) - Inhibition of eosinophil activation through A3 adenosine receptor antagonism (see columns 3-4).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SATYENDRA K. SINGH whose telephone number is (571)272-8790. The examiner can normally be reached on 9-5MF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Satyendra K. Singh/
Examiner, Art Unit 1657

/Irene Marx/
Primary Examiner
Art Unit 1651